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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/656,084	09/06/2000	Barry N. Kreiswirth	19124.0002	8869

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EXAMINER
LY, CHEYNE D

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 01/27/2003

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/656,084	KREISWIRTH ET AL.	
	Examiner	Art Unit	
	Cheyne D Ly	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *November 12, 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1 and 3-37* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *8/ 5 & 11/12, 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's arguments in Paper No. 12, filed August 5, 2002, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.
2. It is acknowledged that claim 2 has been cancelled.
3. Claims herein under examination are claims 1 and 3-37.

IDS

1. All documents listed in Form PTO-1449, Paper No. 13, filed August 5, 2002, have been considered. It is suggested that Applicant include publisher information for documents (textbooks) that are similar to that of Durbin et al. and Gusfield et al. on future PTO-1449 forms.

RESPONSE TO AMENDMENTS

Claim Rejections – 35 U.S.C. § 112, First Paragraph

1. Claims 1 and 3-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is maintained with respect to claims 1 and 3-37, as recited in the previous office action Paper No. 10, mailed April 5, 2002.

2. Specific to Claims 1, 32, and 33, applicant argues that the system of the present invention operates in "real time" because it can receive a stream of data (i.e. DNA sequence data), analyze the data, and send infection control information rapidly enough to allow infection control actions

to be taken to control the spread of the outbreak. Applicant further support the present invention by citing that known method (Pulsed Field Gel Electrophoresis (PFGE) does not allow for real-time infection control because Lencastre et al. reported that the PFGE technique could take as long as 4-5 days or more. Such argument is found unpersuasive because Applicant is comparing the time it takes to generate data in the PFGE method to the transmission of data of the present invention. Applicant seems to be defining "real time" infection control by arguing that the instant application is faster than either the PFGE or MLST, therefore, these techniques do not operate in "real time." Applicant's argument is found unpersuasive. It is noted that Lencastre et al. reported the availability electronic communication systems should provide a quick reportage of the fingerprinting data back to the particular hospitals so that appropriate infection control measures could be instituted (Page 349, Column 2, Lines 15-18). Using Applicant's criteria for considering methods operating in "real time," PFGE could also be considered to operate in "real time."

3. It is reiterated that the specification on page 8 relies upon a known characterized region that is also a fast mutating region in order to accomplish infection control in "real time." However, only identification of a couple characterized regions such as the protein A gene (spa) or coagulase (coa) gene regions of the *Staphylococcus aureus* are disclosed. In addition, nowhere in the claims or the specification is there a clear and direct explanation as to how pathogenic microorganisms without fast mutating regions are to be analyzed for phylogenetic relatedness for real time infection control. Further, it is also noted that "different proteins will have different clock rates, because the metabolic function of some proteins will be much more sensitive to change in their amino acid sequence" (Griffiths et al., Page 2, Lines 33-36 and

Figure 26-17). Thus, a method that relies on regions with a good "clock speed", i.e. regions that mutate not too fast and not too slow, would be unpredictable at best. While, working examples are not, per se, required, the specification must provide adequate guidance such that one of skill in the art could practice the invention without undue experimentation. The specification as originally filed requires undue experimentation by one of skill in the art since methods of infection control analysis for every microorganism are not currently known. Further, the method of the claimed invention relies on molecular clock for proteins that have not all been determined. Given the lack of working examples in the specification, and the unpredictability of real-time infection control in the context of any microorganism, the specification, as filed is not enabling for the method of analyzing any sample microorganism as claimed. Claims 3-31 and 34-37 are rejected for being directly or indirectly dependent from claim 1.

4. Specific to claims 15-18, the instant application fails to provide guidance to one of ordinary skill in the art for generating the following "costs" as recited in claims 15-18: relative cost, absolute cost, repeat motif cost, point mutation cost, and total cost (which is based upon the summation of the repeat cost and point mutation cost). It is acknowledged that applicant points to pages 28-29 for support to overcome the rejection specific to claims 15-18. Examiner has not found any disclosure of the claimed support in pages 28 and 29. It is noted that pages 32 and 33 contain the cited support.

5. Applicant's citation of the specification (pages 32 and 33) that the Examiner found lacking in guidance to one of ordinary skill in the art for generating relative cost, absolute cost, repeat motif cost, point mutation cost, and total cost in the previous office action (See Office Action, Paper No. 10, mailed April 5, 2002) without providing further support is found

unpersuasive. Additionally, Examiner reviewed the excerpts that Applicant alleges contain techniques for measuring phylogenetic costs as disclosed in the specification and found the discussions within the said excerpts to center around gap penalties, deletion cost, insertion cost, and mutation but not relative cost, absolute cost, repeat motif cost, a point mutation cost, or total cost. Therefore, Applicant's argument and references have been considered and they have been found to be unpersuasive.

Claim Rejections – 35 U.S.C. § 112, Second Paragraph

6. Claims 1 and 3-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is maintained with respect to claims 1 and 3-37, as recited in the previous office action Paper No. 10, mailed April 5, 2002.

7. Specific to claims 1, 32 and 33, line 1, it is unclear as to the length of time required for real-time infection control. It is acknowledged that applicant provided adequate support for the description of "real time" within the context of a computer system in Paper No. 12, file August 5, 2002, page 17. However, Applicant emphasized on page 18, that the present invention is an improvement over the methods known in the art such as PFGE or MLST because it is much fast than either method. Further, Applicant proceeded to define "real-time infection control" of the present invention because it is faster than 4-5 days. How fast does a method have to be in order for one to consider it to be operating in "real-time" within the context of infection control? Clarification of the metes and bounds of the instant claims is required. Claims 3-31 and 34-37 are rejected for being directly or indirectly dependent from claim 1.

8. Specific to claims 1, line 9; 32, line 14; 33, line 10, and 37, line 1, it is unclear as to what the applicant regards as information necessary for infection control (See Paper No. 10, mailed April 5, 2002, page 6, 3rd paragraph). It is acknowledged that Applicant amended claim 26 to help differentiate the limitation of the said claim from claims 1, 32 and 33. However, the said amendment does not help resolve the vague and indefiniteness of claims 1, 32 and 33. Claims 3-31 and 34-36 are rejected for being directly or indirectly dependent from claim 1.

9. Specific to claim 3, which depends from claim 1, the said claim lacks a step of sample submission or sample transmission over a network to an infection control facility.

10. Specific to claim 5, line 2, the term "suitably fast" makes the claim vague and indefinite. It is not clear as to what criteria Applicant is using to determine that a specific mutation rate is "suitably fast." It is noted that the description of "suitably fast" is not found on page 18 in the specification. However, Applicant does discuss "clock speed"; i.e. regions that mutate not too fast and not too slow on page 21-22 in the specification. Claim 5 remains vague and indefinite because Applicant does not specify criteria being used to determine that the mutation rate for a specific gene is "suitably fast." Clarification of the metes and bounds of the instant claims is required.

11. Specific to claim 11, lines 3 and 4, the phrase "sensitive patient information" causes the claim to be vague and indefinite. Applicant does not set forth the criteria for determining sensitive patient information. Is patient information sensitive because it may be damaged during transmission or storage, or is it private information regarding the patients? Clarification of the metes and bounds of the instant claims is required.

12. Specific to claims 15 and 16, the step of determining the phylogenetic relatedness between the microorganism sample and a historical sample stored in the database causes the claim to be vague and indefinite. Claim 1 recites a step for determining a measure of phylogenetic relatedness between first sequence region and the historical sequence data. However, claims 15 and 16 recite a step for determining the phylogenetic relatedness between the microorganism sample and a historical sample stored in the database. Applicant does not specify the microorganism sample or the historical sample. Therefore, the lack of specificity causes the claim to be vague and indefinite. Claims 17-20 are rejected for being dependent from claim 16.

13. Specific to claims 22 and 25-27 are vague and indefinite due to the lack of clarity in the step of "transmitting." Due to the lack of computer hardware or computer network requirements in claim 1 from which claims 22 and 25-27 depend, it is unclear as to how the step of transmitting can occur. Claim 23 and 24 is rejected for being dependent from claim 22.

Claim Rejections – 35 U.S.C. § 102

14. Claims 1, 3-7, 9, 12-14, 21, 25-32 and 33-37 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Shopsin et al. (1999). This rejection is maintained with respect to claims 1, 3-7, 9, 12-14, 21, 25-32 and 33-37, as recited in the previous office action Paper No. 10, mailed April 5, 2002.

15. In addition to the limitations cited in previous action (Paper No. 10, file April 5, 2002, Pages 10), Shopsin et al. discloses *S. aureus* typing has become an important tool in the study of strain origin, clonal relatedness, the epidemiology of outbreaks (Page 3556, Column 1, lines 6-7). "Since the major source of variation in the X region seems to be duplication or deletion of the

repetitive units, strain lineages cannot be obtained by comparing the sequences with an algorithm based on sequence alignment. This precludes the use of a dendrogram to visually represent typing results because dendrograms rely on sequence alignments. Therefore, we attempted to establish strain relatedness by first identifying all possible variations of the repeat units and then assessing how these repeat units were organized in the X regions of the different isolates" (Page 3557, Column 2, Lines 22-28). Further, Shopsin et al. discloses "[t]he main advantage of *spa* typing over current methods may be the unambiguity and portability of sequence data. This greatly simplifies the sharing of information between laboratories and facilitates the creation of a large-scale database for the study of global as well as local epidemiology (the electronic portability of sequence data allows rapid exchange of strain typing information without having to transfer bacterial strains)" (Page 3562, column1, lines 54-60). "The requirements for sequence typing are the ability to perform PCR and access to an automated sequencer, both of which are increasingly available to clinical laboratories and public health facilities worldwide."... "Interpretation of the sequence information from *spa* sequencing does not require sophisticated algorithms and utilizes readily available sequence analysis software (GCG Wisconsin Package 9.1) that allows the description of strain types by a simple number code and alphabetical repeat designation. Thus, *spa* typing lends itself to use in a wide range of laboratories as well as the clinical environment" (Page 3562, column 2, lines 6-22). The above disclosure by Shopsin et al. encompasses the limitations as recited in claims 28-31 and new claims 34-37.

16. Applicant argues that the Shopsin article represents the work of the inventors and the other authors of this article, Shopsin, Gomez, Montgomery, Smith, Waddington, Dodge, Bost, and Riehman, performed work at the direction of one or both of the inventors. It is suggested

that Applicant may submit a Katz type of declaration to support the said argument in order to overcome such rejection. (See MPEP § 2132.01)

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 1, 3-14, 21, 22-29, 32 and 33-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shopsin et al. (1999) taken with O'Brien et al (1997) in view of Carroll et al. (PN US 5396227 A).

18. Shopsin et al. is applied as described above and in Paper No. 10, file April 5, 2002, Pages 9-10. However, Shopsin et al. does not demonstrate patient medical history exchange as recited in claims 10 and 11, and patient tracking as recited in claims 22-24.

19. O'Brien et al. teaches a method of comparing "genetic relatedness among *Mycobacterium tuberculosis* isolates recovered from patients with active disease" (Page 387, Column 2, Lines 2-5). Due to the tracking of patients' medical records by Bellvue Hospital and the Department of Health in New York City, patients found not adhering to therapy were quarantined. This displays tracking a patient's physical location as well as the sharing of patient information as recited in claims 10, 11, and 22. Sample analysis of the infected individuals occurred prior confinement in the health care facility as recited in claim 8. The "clinical and demographic features of these patients" (Page 390, column 2, 1st paragraph) were reviewed for population risk factors in addition to determining "ongoing transmission of tuberculosis" (Page 388, column 1, 3rd paragraph) as recited in claim 10.

20. Carroll et al. demonstrates that the physical sensing of an individual is well known in the art. The reference teaches an electronic monitoring system, portable and centralized, that monitors the location of an individual by a transmitter tag (abstract) thus motivating claim 23 and 24.

21. Clearly, a skilled artisan would have been motivated to partake the concept emphasized by Shopsin et al. to perform the genetic relatedness determination method for infection control and apply this new typing system for S. aureus based on the DNA sequencing of the variable region of protein A as an alternative to current techniques for use in research and clinical applications (Page 3562, Column 1, lines 9-12). Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use the method of Shopsin et al. and incorporate into it data in regard to patient history and tracking taught by O'Brien et al. and further modify incorporate into it patient physical tracking as taught by Carroll

et al. Thus, one of ordinary skill in the art would have been motivated to perform the claimed invention with a reasonable expectation of success.

New Matter Rejection - 35 U.S.C. § 112, first paragraph

22. Claims 8 and 35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION.

23. The introduction of "prospective patient" is considered to be new matter. This is a new matter rejection. It is acknowledged that Applicant discloses "patient" throughout the specification. The inclusion of the phrase "prospective patient" changes the scope of the claimed subject matter from patients to anyone who is alive. However, the specification discloses "patients" in the context of hospitals and health care facilities (Background of the invention, lines 1-5), which is different from the scope of claims 8 and 35.

CONCLUSION

24. NO CLAIM IS ALLOWED.

25. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 193), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (703) 308-3880. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

27. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

28. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

C. Dune Ly
1/21/03

ARDIN H. MARSCHEL
PRIMARY EXAMINER